DECLARATION OF MARTIN J. JACOBS UNDER 37 C.F.R. § 1.132

I, Martin J. Jacobs, hereby declare the following.

(1) I received my Bachelor of Science Degree in Chemistry from Illinois Institute of Technology 1969. I received my Doctor of Philosophy Degree in Organic Chemistry from Colorado State University in 1975.

(2) I have extensive experience in the formulation of pharmaceutical drug products for therapeutic use, including formulations involving modafinil.

(3) I am an Formulation Development Scientist in the Formulation Development Department of Cephalon, Inc., the assignee of the present application, and have been employed by Cephalon since July, 1999.

(4) I am a joint inventor of the subject matter claimed in the above-identified application, and generally speaking, claims 1-12 present complexes of a modafinil compound and a cyclodextrin. Claims 13-28, and 35-48 define compositions of a modafinil compound and a cyclodextrin, and claims 29-34 define methods of preparing and using the complexes of a modafinil compound and a cyclodextrin.

(5) I have studied the publication Rambert, F.A. et al., *Neuropschychopharmacology*, **1994**, *10(3S),* 169S ("Rambert"), and in my opinion, Rambert is directed to formulations of modafinil with a hydroxy-propyl-betacyclodextrin solution for intracerbroventicular injection in mice.

(6) I am familiar with the Office Action dated May 6, 2003. I have been involved in the preparation, testing and evaluation of modafinil formulations according to the present invention, and in particular with the effects of various concentrations of cyclodextrin on the aqueous solubilization of modafinil. Based on this work, I have found that the aqueous solubility of modafinil in the modafinil/ hydroxy-propyl-betacyclodextrin mixtures reported in Rambert are less than that disclosed and claimed in the present application.

(7) The Rambert publication teaches aqueous solubilization of a mixture of 100 μg of modafinil in 10 μL of 1% hydroxy-propyl-betacyclodextrin solution, which is equivalent to 10 mg/ml, and a 200 μg of modafinil in 10 μL of 2% hydroxy-propyl-betacyclodextrin solution, which is equivalent to 20 mg/ml.

(8) To confirm the teachings of Rambert, I purchased hydroxy-propyl-betacyclodextrin (tradename Cavitron™) from Eridania Began-Say and prepared 1 and 2% aqueous solutions, by weight. In a first experiment, I found that it was not possible to prepare a 10 mg/ml solution of modafinil in a 2% hydroxy-propyl-betacyclodextrin solution (by weight) at room temperature. Upon heating the solution to 85 °C, the modafinil dissolved; however upon cooling a precipitate formed as early as 50-60 °C. In a second experiment, I attempted to prepare a 5 mg/ml solution of modafinil in a 2% hydroxy-propyl-betacyclodextrin solution (by weight) at room temperature, but was unsuccessful. Upon heating the solution to 87 °C, the modafinil became solubilized, however a precipitate appeared on cooling to approximately 30 °C. In a third experiment, I was able to prepare a fully solubilized 2.5 mg/ml solution of modafinil in 2% hydroxy-propyl-betacyclodextrin solution (by weight) at room temperature.

(9) Thus the experiments demonstrate that modafinil is not fully solubilized at 10 mg/ml in an aqueous 2% hydroxy-propyl-betacyclodextrin solution (by weight) at room temperature.

(10) The aforementioned results are consistent with the aqueous solubilization of a 1:1 mole ratio of modafinil with hydroxy-propyl-betacyclodextrin. By calculation, a 1:1 ratio of modafinil to hydroxy-propyl-betacyclodextrin gives an aqueous solubility of modafinil of about 4.4 mg/ml. Thus, I was unable to completely solubilize modafinil at either 10 mg/ml or 5 mg/ml in an aqueous 2% hydroxy-propyl-betacyclodextrin solution at room temperature, while the 2.5 mg/ml solution did result in fully solubilized modafinil.

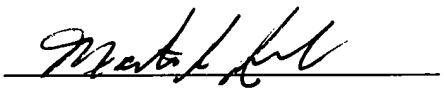
(11) The 200 μg of modafinil in 10 μL of 2% hydroxy-propyl-betacyclodextrin solution as taught in Rambert gives a molar ratio of modafinil: hydroxy-propyl-betacyclodextrin of approximately 5:1.

(12) The foregoing results indicate that preparation of the modafinil: hydroxy-propyl-betacyclodextrin mixtures taught in Rambert could not fully solubilize modafinil at 10 mg/ml in an aqueous 1% or 2% hydroxy-propyl-betacyclodextrin solution. Rather, based on my experience in the lab, preparation of these mixtures lead to precipitates of modafinil, and based on my calculations, the probable solubilization of modafinil in these solutions was less than 5 mg/ml.

(13) In the present patent application, claim 2 is directed to a complex of a modafinil compound and a cyclodextrin wherein the modafinil compound has an aqueous solubilization of at least 10 mg/ml. Claim 9 is directed to an aqueous solubilization of 20 mg/ml. Hence, in my opinion, these claims are distinguishable over the teachings of Rambert.

(14) I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that the statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: November 6, 2003



Martin J. Jacobs